

Serial Number: 09/913,558

CRF Processing Date: 10/11/2001  
 Edited by: A  
 Verified by: A (STIC staff)

**ENTERED**

45

- ☐ Changed a file from non-ASCII to ASCII
- ☐ Changed the margins in cases where the sequence text was "wrapped" down to the next line.
- ☐ Edited a format error in the Current Application Data section, specifically: \_\_\_\_\_
- ☐ Edited the Current Application Data section with the actual current number. The number inputted by the applicant was ☐ the prior application data; or ☐ other \_\_\_\_\_
- ☐ Added the mandatory heading and subheadings for "Current Application Data".
- ☐ Edited the "Number of Sequences" field. The applicant spelled out a number instead of using an integer.
- ☐ Changed the spelling of a mandatory field (the headings or subheadings), specifically: \_\_\_\_\_
- ☐ Corrected the SEQ ID NO when obviously incorrect. The sequence numbers that were edited were: \_\_\_\_\_
- ☐ Inserted or corrected a nucleic number at the end of a nucleic line. SEQ ID NO's edited: \_\_\_\_\_
- ☐ Corrected subheading placement. All responses must be on the same line as each subheading. If the applicant placed a response below the subheading, this was moved to its appropriate place.
- ☐ Inserted colons after headings/subheadings. Headings edited included: \_\_\_\_\_
- ☐ Deleted extra, invalid, headings used by an applicant, specifically: \_\_\_\_\_
- ☒ Deleted: ☒ non-ASCII "garbage" at the beginning/end of files; ☐ secretary initials/filename at end of file;  
☐ page numbers throughout text; ☐ other invalid text, such as \_\_\_\_\_
- ☐ Inserted mandatory headings, specifically: \_\_\_\_\_
- ☐ Corrected an obvious error in the response, specifically: \_\_\_\_\_
- ☐ Edited identifiers where upper case is used but lower case is required, or vice versa.
- ☐ Corrected an error in the Number of Sequences field, specifically: \_\_\_\_\_
- ☐ A "Hard Page Break" code was inserted by the applicant. All occurrences had to be deleted.
- ☐ Deleted *ending* stop codon in amino acid sequences and adjusted the "(A)Length:" field accordingly (error due to a PatentIn bug). Sequences corrected: \_\_\_\_\_
- ☐ Other: \_\_\_\_\_

Examiner: The above corrections must be communicated to the applicant in the first Office Action. DO NOT send a copy of this form.

3/1/95

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/913,558

DATE: 10/11/2001

TIME: 10:47:15

Input Set : A:\PTO.AMC.txt

Output Set: N:\CRF3\10112001\I913558.raw

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5 <110> APPLICANT: Brett P. Monia
6     Lex M. Cowsert
7     ISIS PHARMACEUTICALS, INC.
9 <120> TITLE OF INVENTION: ANTISENSE MODULATION OF SMAD5 EXPRESSION
11 <130> FILE REFERENCE: RTSP-0161
C--> 13 <140> CURRENT APPLICATION NUMBER: US/09/913,558
C--> 14 <141> CURRENT FILING DATE: 2001-08-15
16 <150> PRIOR APPLICATION NUMBER: US 09/256,492
17 <151> PRIOR FILING DATE: 1999-02-23
19 <160> NUMBER OF SEQ ID NOS: 47
21 <210> SEQ ID NO: 1
22 <211> LENGTH: 1597
23 <212> TYPE: DNA
24 <213> ORGANISM: Homo sapiens
26 <220> FEATURE:
27 <221> NAME/KEY: CDS
28 <222> LOCATION: (150)..(1547)
30 <400> SEQUENCE: 1
31 gcataatggca cttgtgaaga taaatgttac tcctcccttt ttaattggaa cttctgctta      60
33 ggacctgtgt atgacgtttc acctgtgatc tgttctttcg gtagccactg actttgagtt      120
35 acaggaaggt ctccgaagat ttgtgtcaa atg acg tca atg gcc agc ttg ttt      173
36                                     Met Thr Ser Met Ala Ser Leu Phe
37                                     1                               5
39 tct ttt act agt cca gca gta aag cga ttg ttg ggc tgg aaa caa ggt      221
40 Ser Phe Thr Ser Pro Ala Val Lys Arg Leu Leu Gly Trp Lys Gln Gly
41 10                               15                               20
43 gat gag gag gag aaa tgg gca gaa aag gca gtt gat gct ttg gtg aag      269
44 Asp Glu Glu Glu Lys Trp Ala Glu Lys Ala Val Asp Ala Leu Val Lys
45 25                               30                               35                               40
47 aaa cta aaa aag aaa aag ggt gcc atg gag gaa ctg gag aaa gcc ttg      317
48 Lys Leu Lys Lys Lys Lys Gly Ala Met Glu Glu Leu Glu Lys Ala Leu
49 45                               50                               55
51 agc agt cca gga cag ccg agt aaa tgt gtc act att ccc aga tct tta      365
52 Ser Ser Pro Gly Gln Pro Ser Lys Cys Val Thr Ile Pro Arg Ser Leu
53 60                               65                               70
55 gat gga cgc ctg cag gtt tct cac aga aaa ggc tta ccc cat gtt ata      413
56 Asp Gly Arg Leu Gln Val Ser His Arg Lys Gly Leu Pro His Val Ile
57 75                               80                               85
59 tat tgt cgt gtt tgg cgc tgg ccg gat ttg cag agt cat cat gag cta      461
60 Tyr Cys Arg Val Trp Arg Trp Pro Asp Leu Gln Ser His His Glu Leu
61 90                               95                               100
63 aag ccg ttg gat att tgt gaa ttt cct ttt gga tct aag caa aaa gaa      509
64 Lys Pro Leu Asp Ile Cys Glu Phe Pro Phe Gly Ser Lys Gln Lys Glu
65 105                               110                               115                               120
67 gtt tgt atc aac cca tac cac tat aag aga gtg gag agt cca gtc tta      557
68 Val Cys Ile Asn Pro Tyr His Tyr Lys Arg Val Glu Ser Pro Val Leu
69 125                               130                               135

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71	cct cca gta tta gtg cct cgt cat aat gaa ttc aat cca caa cac agc	605
72	Pro Pro Val Leu Val Pro Arg His Asn Glu Phe Asn Pro Gln His Ser	
73	140 145 150	
75	ctt ctg gtt cag ttt agg aac ctg agc cac aat gaa cca cac atg cca	653
76	Leu Leu Val Gln Phe Arg Asn Leu Ser His Asn Glu Pro His Met Pro	
77	155 160 165	
79	caa aat gcc acg ttt cca gat tct ttc cac cag ccc aac aac act cct	701
80	Gln Asn Ala Thr Phe Pro Asp Ser Phe His Gln Pro Asn Asn Thr Pro	
81	170 175 180	
83	ttt ccc tta tct cca aac agc cct tat ccc cct tcg cct gct agc agc	749
84	Phe Pro Leu Ser Pro Asn Ser Pro Tyr Pro Pro Ser Pro Ala Ser Ser	
85	185 190 195 200	
87	aca tat ccc aac tcc cca gca agt tct gga cca gga agt cca ttt cag	797
88	Thr Tyr Pro Asn Ser Pro Ala Ser Ser Gly Pro Gly Ser Pro Phe Gln	
89	205 210 215	
91	ctc cca gct gat acg cct cct cct gcc tat atg cca cct gat gat cag	845
92	Leu Pro Ala Asp Thr Pro Pro Pro Ala Tyr Met Pro Pro Asp Asp Gln	
93	220 225 230	
95	atg ggt caa gat aat tcc cag cct atg gat aca agc aat aat atg att	893
96	Met Gly Gln Asp Asn Ser Gln Pro Met Asp Thr Ser Asn Asn Met Ile	
97	235 240 245	
99	cct cag att atg ccc agt ata tcc agc agg gat gtt cag cct gtt gcc	941
100	Pro Gln Ile Met Pro Ser Ile Ser Ser Arg Asp Val Gln Pro Val Ala	
101	250 255 260	
103	tat gaa gag cct aaa cat tgg tgt tca ata gtc tac tat gaa tta aac	989
104	Tyr Glu Glu Pro Lys His Trp Cys Ser Ile Val Tyr Tyr Glu Leu Asn	
105	265 270 275 280	
107	aat cgt gtt gga gaa gct ttt cat gca tct tct act agt gtg tta gta	1037
108	Asn Arg Val Gly Glu Ala Phe His Ala Ser Ser Thr Ser Val Leu Val	
109	285 290 295	
111	gat gga ttc aca gat cct tca aat aac aaa agt aga ttc tgc ttg ggt	1085
112	Asp Gly Phe Thr Asp Pro Ser Asn Asn Lys Ser Arg Phe Cys Leu Gly	
113	300 305 310	
115	ttg ttg tca aat gtt aat cgt aat tcg aca att gaa aac act agg cga	1133
116	Leu Leu Ser Asn Val Asn Arg Asn Ser Thr Ile Glu Asn Thr Arg Arg	
117	315 320 325	
119	cat att gga aaa ggt gtt cat ctg tac tat gtt ggt gga gag gtg tat	1181
120	His Ile Gly Lys Gly Val His Leu Tyr Tyr Val Gly Gly Glu Val Tyr	
121	330 335 340	
123	gcg gaa tgc ctc agt gac agc agc ata ttt gta cag agt agg aac tgc	1229
124	Ala Glu Cys Leu Ser Asp Ser Ser Ile Phe Val Gln Ser Arg Asn Cys	
125	345 350 355 360	
127	aac ttt cat cat ggc ttt cat ccc acc act gtc tgt aag att ccc agc	1277
128	Asn Phe His His Gly Phe His Pro Thr Thr Val Cys Lys Ile Pro Ser	
129	365 370 375	
130	agc tgc agc ctc aaa att ttt aac aat cag gag ttt gct cag ctt ctg	1325
131	Ser Cys Ser Leu Lys Ile Phe Asn Asn Gln Glu Phe Ala Gln Leu Leu	
132	380 385 390	
134	gct caa tct gtc aac cat ggg ttt gag gca gta tat gag ctc acc aaa	1373

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135 Ala Gln Ser Val Asn His Gly Phe Glu Ala Val Tyr Glu Leu Thr Lys
136          395          400          405
138 atg tgt acc att cgg atg agt ttt gtc aag ggt tgg gga gca gaa tat      1421
139 Met Cys Thr Ile Arg Met Ser Phe Val Lys Gly Trp Gly Ala Glu Tyr
140      410          415          420
142 cac cgg cag gat gta acc agc acc cca tgt tgg att gag att cat ctt      1469
143 His Arg Gln Asp Val Thr Ser Thr Pro Cys Trp Ile Glu Ile His Leu
144 425          430          435          440
146 cat ggg cct ctt cag tgg ctg gat aaa gtc ctt act cag atg ggc tcc      1517
147 His Gly Pro Leu Gln Trp Leu Asp Lys Val Leu Thr Gln Met Gly Ser
148          445          450          455
150 cct ctg aac ccc ata tct tct gtt tca taa tgcagaagta ttcttttcaa      1567
151 Pro Leu Asn Pro Ile Ser Ser Val Ser
152          460          465
154 ttatatattggt agtggacttg ttttaatttt      1597
157 <210> SEQ ID NO: 2
158 <211> LENGTH: 21
159 <212> TYPE: DNA
160 <213> ORGANISM: Artificial Sequence
162 <220> FEATURE:
163 <223> OTHER INFORMATION: PCR Primer
165 <400> SEQUENCE: 2
166 cagcaagttc tggaccagga a      21
169 <210> SEQ ID NO: 3
170 <211> LENGTH: 23
171 <212> TYPE: DNA
172 <213> ORGANISM: Artificial Sequence
174 <220> FEATURE:
175 <223> OTHER INFORMATION: PCR Primer
177 <400> SEQUENCE: 3
178 ccatctgatc atcaggtggc ata      23
181 <210> SEQ ID NO: 4
182 <211> LENGTH: 26
183 <212> TYPE: DNA
184 <213> ORGANISM: Artificial Sequence
186 <220> FEATURE:
187 <223> OTHER INFORMATION: PCR Probe
189 <400> SEQUENCE: 4
190 tccatttcag ctcccagctg atacgc      26
193 <210> SEQ ID NO: 5
194 <211> LENGTH: 19
195 <212> TYPE: DNA
196 <213> ORGANISM: Artificial Sequence
198 <220> FEATURE:
199 <223> OTHER INFORMATION: PCR Primer
201 <400> SEQUENCE: 5
202 gaaggtgaag gtcggagtc      19
205 <210> SEQ ID NO: 6
206 <211> LENGTH: 20

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207 <212> TYPE: DNA
208 <213> ORGANISM: Artificial Sequence
210 <220> FEATURE:
211 <223> OTHER INFORMATION: PCR Primer
213 <400> SEQUENCE: 6
214 gaagatggtg atgggatttc                20
217 <210> SEQ ID NO: 7
218 <211> LENGTH: 20
219 <212> TYPE: DNA
220 <213> ORGANISM: Artificial Sequence
222 <220> FEATURE:
223 <223> OTHER INFORMATION: PCR Probe
225 <400> SEQUENCE: 7
226 caagcttccc gttctcagcc                20
229 <210> SEQ ID NO: 8
230 <211> LENGTH: 18
231 <212> TYPE: DNA
232 <213> ORGANISM: Artificial Sequence
234 <220> FEATURE:
235 <223> OTHER INFORMATION: Antisense Oligonucleotide
237 <400> SEQUENCE: 8
238 ttatcttcac aagtgccca                18
241 <210> SEQ ID NO: 9
242 <211> LENGTH: 18
243 <212> TYPE: DNA
244 <213> ORGANISM: Artificial Sequence
246 <220> FEATURE:
247 <223> OTHER INFORMATION: Antisense Oligonucleotide
249 <400> SEQUENCE: 9
250 ctaagcagaa gttccaat                18
253 <210> SEQ ID NO: 10
254 <211> LENGTH: 18
255 <212> TYPE: DNA
256 <213> ORGANISM: Artificial Sequence
258 <220> FEATURE:
259 <223> OTHER INFORMATION: Antisense Oligonucleotide
261 <400> SEQUENCE: 10
262 tcatacacag gtcctaag                18
265 <210> SEQ ID NO: 11
266 <211> LENGTH: 18
267 <212> TYPE: DNA
268 <213> ORGANISM: Artificial Sequence
270 <220> FEATURE:
271 <223> OTHER INFORMATION: Antisense Oligonucleotide
273 <400> SEQUENCE: 11
274 aagaacagat cacagggtg                18
277 <210> SEQ ID NO: 12
278 <211> LENGTH: 18
279 <212> TYPE: DNA

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Input Set : A:\PTO.AMC.txt

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280 <213> ORGANISM: Artificial Sequence  
282 <220> FEATURE:  
283 <223> OTHER INFORMATION: Antisense Oligonucleotide  
285 <400> SEQUENCE: 12  
286 aactcaaagt cagtggct 18  
289 <210> SEQ ID NO: 13  
290 <211> LENGTH: 18  
291 <212> TYPE: DNA  
292 <213> ORGANISM: Artificial Sequence  
294 <220> FEATURE:  
295 <223> OTHER INFORMATION: Antisense Oligonucleotide  
297 <400> SEQUENCE: 13  
298 ttcggagacc ttcctgta 18  
301 <210> SEQ ID NO: 14  
302 <211> LENGTH: 18  
303 <212> TYPE: DNA  
304 <213> ORGANISM: Artificial Sequence  
306 <220> FEATURE:  
307 <223> OTHER INFORMATION: Antisense Oligonucleotide  
309 <400> SEQUENCE: 14  
310 tttgacacaa atcttcgg 18  
313 <210> SEQ ID NO: 15  
314 <211> LENGTH: 18  
315 <212> TYPE: DNA  
316 <213> ORGANISM: Artificial Sequence  
318 <220> FEATURE:  
319 <223> OTHER INFORMATION: Antisense Oligonucleotide  
321 <400> SEQUENCE: 15  
322 acaatcgctt tactgctg 18  
325 <210> SEQ ID NO: 16  
326 <211> LENGTH: 18  
327 <212> TYPE: DNA  
328 <213> ORGANISM: Artificial Sequence  
330 <220> FEATURE:  
331 <223> OTHER INFORMATION: Antisense Oligonucleotide  
333 <400> SEQUENCE: 16  
334 atcaccttgt ttccagcc 18  
337 <210> SEQ ID NO: 17  
338 <211> LENGTH: 18  
339 <212> TYPE: DNA  
340 <213> ORGANISM: Artificial Sequence  
342 <220> FEATURE:  
343 <223> OTHER INFORMATION: Antisense Oligonucleotide  
345 <400> SEQUENCE: 17  
346 catttctcct cctcatca 18  
349 <210> SEQ ID NO: 18  
350 <211> LENGTH: 18  
351 <212> TYPE: DNA  
352 <213> ORGANISM: Artificial Sequence

## VERIFICATION SUMMARY

DATE: 10/11/2001

PATENT APPLICATION: US/09/913,558

TIME: 10:47:16

Input Set : A:\PTO.AMC.txt

Output Set: N:\CRF3\10112001\I913558.raw

L:13 M:270 C: Current Application Number differs, Replaced Application Number

L:14 M:271 C: Current Filing Date differs, Replaced Current Filing Date